AN INQUIRY INTO THE NATURE OF THE SKELETAL CHANGES IN ACROMEGALY

BY

ARTHUR KEITH, M.D. ABERD., F.R.C.S. ENG.,

CONSERVATOR OF THE MUSEUM OF THE ROYAL COLLEGE OF SURGEONS OF ENGLAND.

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AN INQUIRY INTO THE NATURE OF THE SKELETAL CHANGES IN ACROMEGALY.[1]

I WAS drawn into the study of acromegaly by an accident. While revising the series of specimens which illustrate variations of the skull in the Museum of the Royal College of Surgeons of England my attention was drawn to one which illustrated over-development of cranial characters On closer examination it became apparent that this skull showed the features of acromegaly, a diagnosis which was confirmed by my colleague Mr. S G. Shattock. The sella turcica, although showing no signs of a tumour, was large, measuring 20 mm. in its front-to-back diameter, 20 mm. from side to side, and 7 mm. in depth; the corresponding measurements in normal male skulls are 10 to 12 mm., 14 to 15 mm., and 8 mm.[2] In a case adjoining that in which the series illustrating variations of the skull is placed are shown the cranial forms of Paleolithic man—the most ancient type of European yet discovered and best known by the specimen found at Neanderthal in 1857. In this series is also placed the Gibraltar cranium which was brought home by a former President of the College, Mr. George Busk, and presented by him to the Museum in 1868. On searching the records of the Gibraltar Scientific Society last year Colonel Kenyon, R.E., came across an entry which shows that the Gibraltar cranium was discovered in 1848, nine years before the Neanderthal example, which is usually regarded as the first known representative of Paleolithic (Neanderthaloid) man.

[1] A paper read before the Medical Society of London on Dec. 12th 1910, in conjunction with a paper on Acromegaly by Sir David Ferrier (see THE LANCET, Dec. 17th, 1910, p. 1765).

[2] See Boyce, R., and Beadles, C., Journal of Pathology and Bacteriology, 1893, p. 1; Beadles, Cecil, Edinburgh Medical Journal, March-April, 1898; Fitzgerald, D. P., Journal of Anatomy and Physiology, 1910, vol. xliv., p. 231; and Erdheim. J., and Stumme, E., Beiträge zur Pathologischen Anatomie, Ziegler, 1909, Band xlvi., p. 1.

The Resemblance of Acromegalic to Neanderthaloid Crania.

That is a side issue, however; the main point is the marked resemblance of the acromegalic and Neanderthaloid crania; in both types the skulls are particnlarly long and low in proportion to the length; the eyebrow ridges are prominent; the muscular markings are pronounced; in both, the facial parts of the skull are long and wide. The resemblance is close enough to suggest the possibility of obtaining some light on the nature of Neanderthal man by studying the remarkable disease known to medical men as acromegaly. If a pathological disturbance of the pituitary could produce the one condition it seemed possible that a heightened physiological development might produce the other. Those most familiar with craniological methods know best how empirical they are and the need of applying more rational principles to the elucidation of the problems of head form. Acromegaly seems to offer a clue to some of the circumstances which determine the shape of head and face.

The Theory that Acromegaly is an Atavistic Manifestation.

The detection of a resemblance between the Neanderthaloid and acromegalic crania is not a new observation. A brief history of the acromegalic skull which I have already alluded to will make clear how old the suggestion is. The specimen came into the possession of the celebrated craniologist, Dr. Barnard Davis,[3] about the middle of last century; before then it was part of the stock-in-trade of a phrenologist in the Strand. In 1863, when Huxley[4] brought the primitive nature of the Neanderthal cranium before the British public by a masterly analysis of its characters, Dr. Barnard Davis produced the phrenological skull as proof that a similar formation could be found amongst modern men. That was nearly 30 years before the condition of acromegaly was recognised; Pierre Marie's[5] classical description appeared in 1886. Dr. Barnard Davis had recognised the resemblance between the head form of Neanderthal man and that of the acromegalic. The chief features of the Neanderthaloid and acromegalic skulls are also seen in the chimpanzee's and especially in the gorilla's skull. Hence Dr. W. A. Freund,[6] the veteran physician of Berlin, when he described a case of acromegaly in 1872 under the name of *Macrosomia partialis*, definitely mentions the anthropoid nature of the cranial characters of the acromegalic and inclines to the belief that they are a re-appearance of ancestral traits. The influence

[3] Davis, Barnard: Thesaurus Craniorum, 1867, p. 48.
[4] Huxley, T.: Man's Place in Nature, London, 1863.
[5] Marie, Pierre: Revue de Médecine, 1886, vol. vi., p. 297.
[6] Freund, W. A., Sammlung Klinischer Vorträge, 1889, Gynaekologie, No. 95.

of Darwin is there seen at work. Later, Professor D. J. Cunningham,[7] who gave the first (1878) full description of a case of acromegaly in this country, and was also the first to recognise the relationship between acromegaly and giantism, was struck by the anthropoid nature of the acromegalic cranial characters. Dr. Woods Hutchinson,[8] while emphasising the part played by the pituitary secretion in regulating growth of the body, and Dr. Harry Campbell [9] formed opinions somewhat similar to those of Freund and Cunningham.

The Theory of Hyperpituitarism.

The authorities who have written monographs on acromegaly have one and all of them put aside the views advanced by the writers just cited as scarcely worthy of serious consideration. There is a justification for this attitude, for to say that acromegaly is an atavism helps very little to explain the condition. I do not for a minute suggest that the Neanderthaloid race suffered from acromegaly, nor that acromegaly is a resurrection of an anthropoid state. From what is known of the function of the pituitary it may be stated with some degree of assurance that all three—the gorilla, Neanderthal man, and the acromegalic—suffer from that condition which is now known as *hyperpituitarism*,[10] as distinguished from the opposite condition, *hypopituitarism*, where the pituitary secretion falls far below the normal amount. Something is now known of the conditions which stimulate the pituitary to growth and over-secretion. Pregnancy does so; so do castration and thyroidectomy. With the excess of function called forth by these conditions certain growth changes appear in the body of the individual.

The evidence which I propose to bring forward in this paper suggests that at least one of the substances secreted by the anterior or glandular part of the pituitary body is of the nature of a hormone. It renders the osteoblasts hypersensitive to the various stresses which fall on the human skeleton during life. Thus the osteoblasts at the origins and insertions of muscles become increasingly sensitive to the

[7] Cunningham, D. J., Journal of Anatomy and Physiology, 1878, vol. xii., p. 294. The same skeleton was fully described by Professor Alexis Thomson in the Journal of Anatomy and Physiology, 1890, vol. xxiv., p. 475.

[8] Hutchinson, Woods, New York Medical Journal, 1900, July 21st, p. 89.

[9] Campbell, Harry, Brit. Med. Jour., 1894, vol. ii., p. 1110, 1895, vol. i., p. 81.

[10] For summaries of our present knowledge of the nature of acromegaly see Sir David Ferrier's paper in THE LANCET, Dec. 17th, 1910, p. 1765; Dr. A. Münzer, Berliner Klinische Wochenschrift, 1910, Band xlvii., p. 341; Dr. Alfred Kohn, Münchener Medizinische Wochenschrift, 1910, vol. lvii., p. 1485; Professor Sternberg's article in Nothnagel's Specielle Pathologie und Therapie. 1897, vol. vii., p. 11; Dr. Harvey Cushing, Journal of the American Medical Association, 1909, vol. liii., p. 249; and the American Journal of Physiology, 1910, vol. xxvii., p. 60.

traction of the muscle fibres ; the muscular impressions and processes of the skeleton become unduly raised, extended, and emphasised by the formation of new bony matter. The parts and articular surfaces of bones exposed to repeated pressure or tension become the seats of growth.[11] If the epiphyseal lines, the osteoblasts of which appear to be

FIG. 1.

The pituitary fossa of O'Brien's skull (natural size). *a*, Foramen cæcum ; *b*, Crista ; *c*, Cribriform plates ; *d*, *e*, Ridge and fossa caused by impression of pituitary tumour on presphenoid ; *f*, Optic foramen ; *g*, Anterior clinoid processes ; *h*, Petrous bone ; *i*, Dorsum sellæ.

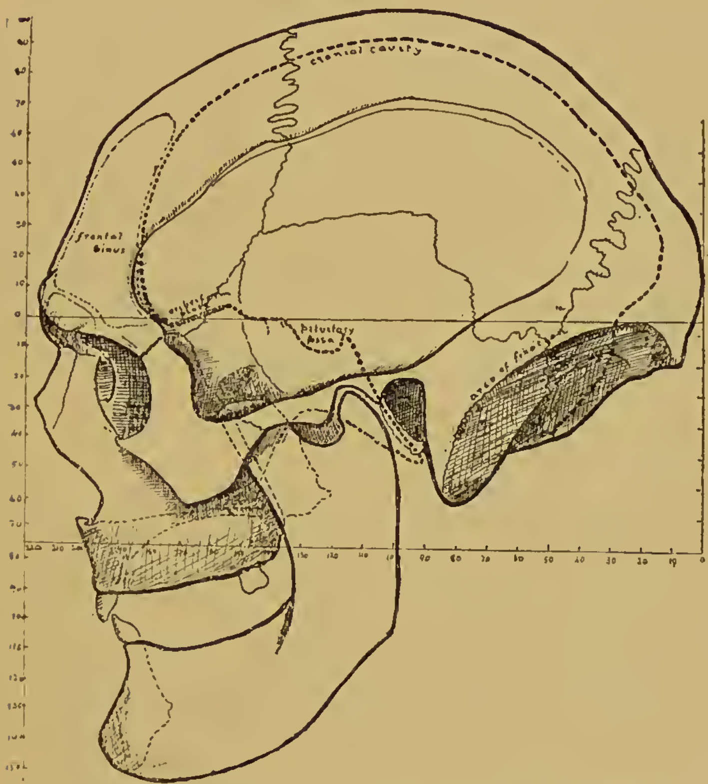
especially affected, are still open, giantism is produced. It is not clearly enough recognised that bone formation is intimately associated with bone absorption. Hunter's[12]

[11] See Mr. F. G. Parsons, Papers on Traction and Pressure Epiphyses in the Journal of Anatomy and Physiology, 1904, vol. xxxviii., p. 248, vol. xlii., p. 388.

[12] Hunter, John, Collective Works (Palmer's Ed.), vol. iv., p. 316.

description of the growth of the femur will be remembered; as the bone grows in length deposition occurs along the upper surface of the neck and head, absorption along the lower. Thus the head and neck of the femur are laid down and completely absorbed several times during the growth of the individual. In acromegaly we see this coördination between growth and absorption is lost to a certain degree; indeed, especially in the later stages, absorption is more marked than deposition. The pituitary

FIG. 2.

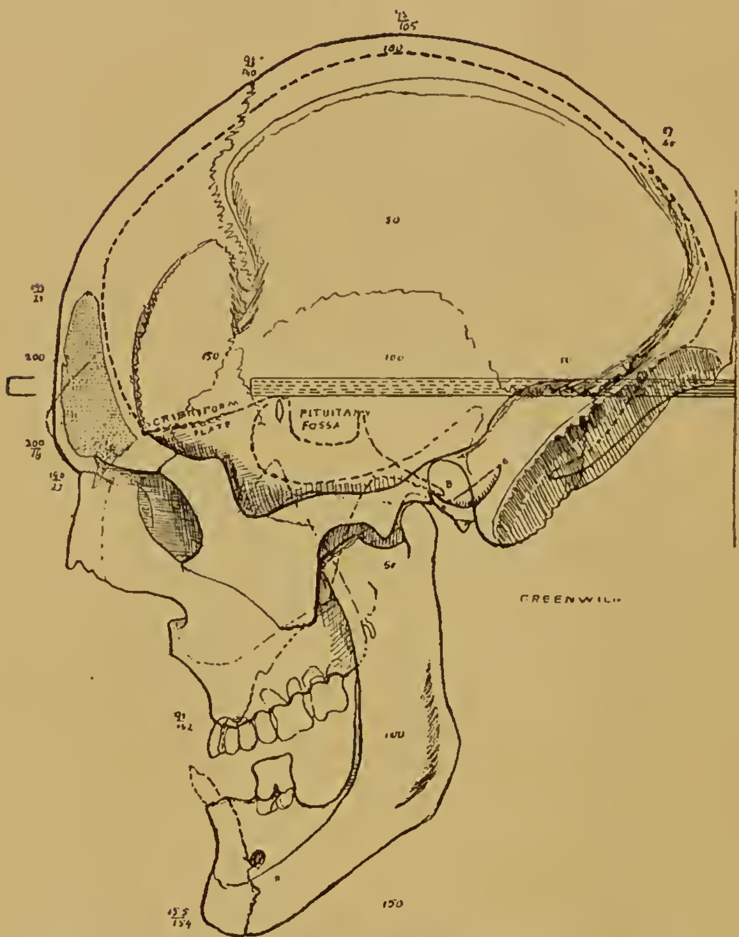


A profile construction of O'Brien's skull showing the outline of the cranial cavity, frontal sinus, and palate (two-fifths natural size). The temporal lines extend anterior to the frontal poles of the brain.

is functionally connected with coördination of the processes of deposition and absorption of bone during the growth of the skeleton; in acromegaly an imperfect process of growth is again awakened; the awakening is apparently due to a hypersecretion of the pituitary.

The new deposit of osseous matter does not depend apparently on the pituitary secretion. Osteoblasts may be stimulated to lay down new bone in many ways. In osteitis deformans (Paget's disease) the deposit of new bone is

FIG. 3.



Profile reconstruction of the acromegalic cranium in the Museum of the Seamen's (Dreadnought) Hospital, Greenwich (two-fifths natural size). The bar seen to perforate the skull marks the plane on which the cranium was orientated. The plane corresponds to the lower border of the cerebrum.

profuse and subperiosteal ; it may be, as Arbuthnot Lane[13] suggested, that the absorption of the old bone is the circumstance which calls forth the profuse deposit

13 Lane, W. Arbuthnot, THE LANCET, April 28th, 1888, p. 815.

of new bone. In osteitis deformans the processes of absorption and deposit are altogether different from that which takes place in acromegaly and normal growth ; the new bone is laid down as a porous subperiosteal layer ; the old bone everywhere undergoes absorption ; there is no resemblance between this pathological process and the normal one of growth. In Paget's disease the osteoblasts have lost one of their most remarkable properties—that of being sensitive to the forces which act on the bones. This property or function of the osteoblasts must be one of their earliest specialisations. Mr. W. Woodland [14] has shown that the scleroblasts which form the spicules of sponges lay down the skeletal elements in conformity with the movements of the surrounding water. Whatever the nature of the cause of Paget's disease may be it is one which deprives the osteoblasts of what may be called their architectural function. In acromegaly the architectural function is not lost; bone is laid down so as to meet the pressures and tensions of the muscles and ligaments and of gravity. Indeed, they become increasingly sensitive to such stimuli. By the twenty-fifth year they have almost ceased to react in normal individuals except when the work of the muscles and strain of the ligaments are greatly exaggerated. In acromegaly they are rendered so sensitive that they react to stimuli which, in normal individuals, would be ineffective.

Material Available for Study in London.

Only those who have taken considerable trouble know how extensive the literature dealing with acromegaly has become. In 1898 Mr. Percy Furnivall [15] was able to collect post-mortem descriptions of 48 cases. Sternberg [16] states that he had collected records of 210 cases. At the present time it would be possible to collect a list of 400 recorded cases. In this great literature there is nowhere to be found an exact inquiry into the nature of the growth changes of the skeleton, particularly of the skull. My intention in writing now is to make good this blank. In the Museum of the College of Surgeons, England, there are the following specimens of acromegaly :—

1. The skull and skeleton of the giant O'Brien. Professor Cunningham was the first to recognise that Hunter's famous giant, obtained at great cost and trouble, was the subject of acromegaly. The condition of the pituitary fossa is shown in Fig. 1 ; it is greatly enlarged, measuring 21 mm. antero-posteriorly, 24 mm. from side to side, and 11 mm. in

[14] Woodland, W.: Quarterly Journal of Microscopical Science, 1905, p. 251; 1906, p. 533.

[15] Furnivall, P.: Transactions of the Pathological Society of London, 1898, vol. xliv., p. 204.

[16] Sternberg, M.: loc. cit.

depth. There had been clearly a tumour of the pituitary, a process of which had grown upwards and forwards, causing a very distinct impression on the floor of the cranial cavity (Fig. 1) between the optic groove and cribriform plates. O'Brien is clearly an example of an acromegalic giant, and suffered from a tumour of the pituitary. He died in 1783 at the age of 22 ; the stature of his skeleton is 7 ft. 8¾ in. (2354 mm.).

2. The acromegalic skull already mentioned as belonging to the Barnard Davis series. This also I believe has been obtained from an acromegalic giant.

3. An acromegalic skull of a man which Mr. Shattock recognised in the collection of Italian crania acquired by the College from Professor Nicolucci in 1870. It is now shown in the pathological series. The pituitary fossa has been enlarged by a tumour ; it measures 20 × 17 × 20 mm. deep.

4. A cranium presented to the College by Mr. Thomson Walker. It is a woman's skull and was acquired in Vienna. It shows an irregular or uncommon type of acromegaly, in some points resembling the cranial lesions seen in Paget's disease. The pituitary has been the seat of a tumour ; the fossa measures 19 × 22 × 14 mm.

5. The calvarium of an insane acromegalic woman, aged 40 years, presented by Mr. Cecil Beadles [17] in 1907. In this case there was a tumour of the pituitary.

6. Pituitary tumour, *in situ*, of a case recorded by Mr. J. Breward Neal and Mr. S. G. Shattock. [18]

Besides the material in the College Museum I was fortunate in obtaining access to the following specimens.

1. A remarkable cranium of a man in the Museum of the Seamen's (Dreadnought) Hospital, Greenwich. The specimen is mentioned by Mr. Richard Partridge in his article on the Face in "Todd's Encyclopædia of Anatomy and Physiology," Vol. II., p. 219, 1839. The pituitary fossa is uniformly enlarged and measures 21 × 23 × 11 mm. The age of the man, a native of Shields, is unknown, but I estimate from the condition of the skull that he was between 50–60 years.

2. In the Museum of St. Bartholomew's Hospital there are specimens from three cases of acromegaly, including the case described by Mr. P. Furnivall in 1898. There is also there the skeleton of a negro who evidently was the subject of acromegaly or a nearly allied condition. The stature estimated from the skeleton is 1910 mm. ; certain of the digits are hypertrophied ; the bones of the skull are dense and thick ; the bones show changes recalling the lesions seen in acromegaly. The number of the specimen is 298. His leg was amputated by Mr. Earle on account of a condition which was diagnosed as syphilis. The pituitary fossa is slightly

[17] See Edinburgh Medical Journal, 1898, p. 501.
[18] Transactions of the Pathological Society of London, vol. xlix., p. 224.

enlarged, measuring 19 mm. back to front, 12 side to side, and 8 in depth.

3. In the London Hospital Museum there is a series of pituitary tumours, one of which was removed from a case of Dr. T. W. Chevalier in 1827. The description of this case,[19] that of a woman aged 39 years, leaves no doubt as to the nature of the disease. So far as I know Dr. Chevalier's is the first complete description of acromegaly in this country. There is also in the same museum the skeleton of the only non-acromegalic giant in London. The skeleton measures 2170 mm. (7 ft. 2 in.), and the pituitary fossa is only slightly enlarged, measuring 15 × 18 × 6 mm. Mr. T. Openshaw, who at great trouble prepared and articulated this very valuable specimen, informs me that the skeleton is that of a Chinaman who died in London in 1880 and was about 50 years of age. He died from broncho-pneumonia in the City of London Sick Asylum. There are also in the same museum the skeleton and casts of the "elephant" man described by Sir Frederick Treves.[20] The condition, although unilateral, is certainly one closely allied to acromegaly.

4. In the Museum attached to Charing Cross Hospital there are casts of the face and hands and representative parts of the case described by Dr. William Hunter.[21]

5. In the Museum of St. Mary's Hospital there are two specimens, not of acromegaly but of closely allied diseases. One is a case of leontiasis ossea; the other exemplifies a condition which is evidently a distinct morbid entity and deserves a fuller description than can be given here. The pituitary fossa is deformed and the condition of the skull shows characters which ally it to acromegaly on the one hand and oxycephaly on the other.

6. I had also the opportunity of examining, in the Museum of Edinburgh University, the skeleton of the case of acromegaly first described by Professor Cunningham in 1878, and 10 years later, in a more detailed manner, by Professor Alexis Thomson.

Growth Changes in the Palate.

In acromegaly there is no increase in the area of the palate. By the palatal area is meant the space bounded anteriorly and at the sides by the outer alveolar margin, and behind by a base line drawn from one side of the palate to the other behind the last molar tooth. (Fig. 4.) The area has a physiological significance; its extent depends on the roughness and quantity of the food. Fig. 4 shows the manner in which the size of the palate is estimated; the outline is

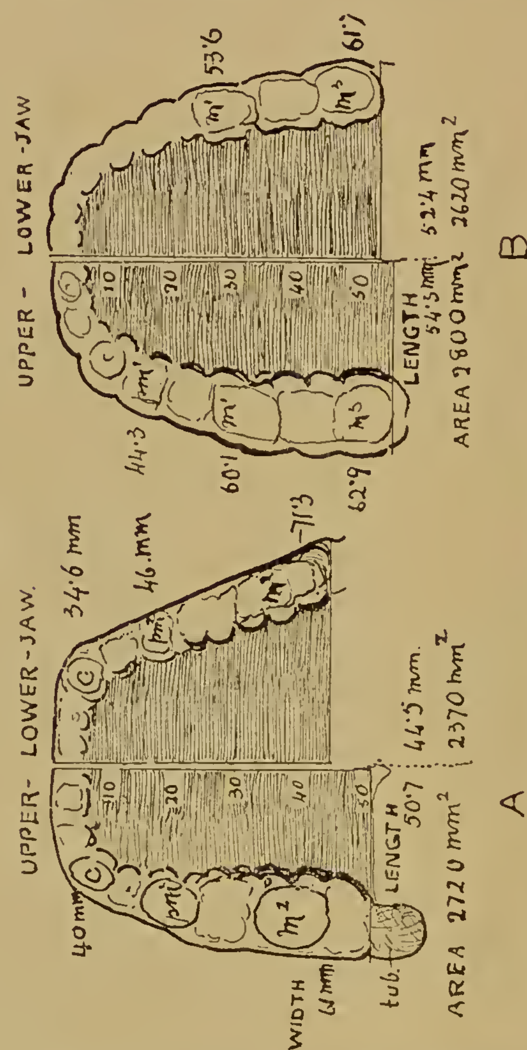
[19] Chevalier, T. W.: London Medical and Physical Journal, 1827, vol. lviii., p. 498.

[20] Treves, Sir Frederick: The Lancet, March 21st, 1885, p. 519.

[21] Hunter, W.: Transactions of the Pathological Society of London, 1898, vol. xlix., p. 246.

traced on millimetre paper and the enclosed area estimated. In Fig. 4 A are shown the areas enclosed by the upper and lower alveolar arcades of the acromegalic. The figures are founded on measurements made on six cases of acromegaly. In Fig. 4 B the corresponding areas in normal individuals are

FIG. 4.



The mean area of the upper and lower alveolar arcades. A, In acromegaly (6 cases). B, In English medical students (21 individuals). The mean measurements for length and breadth are given on the figures.

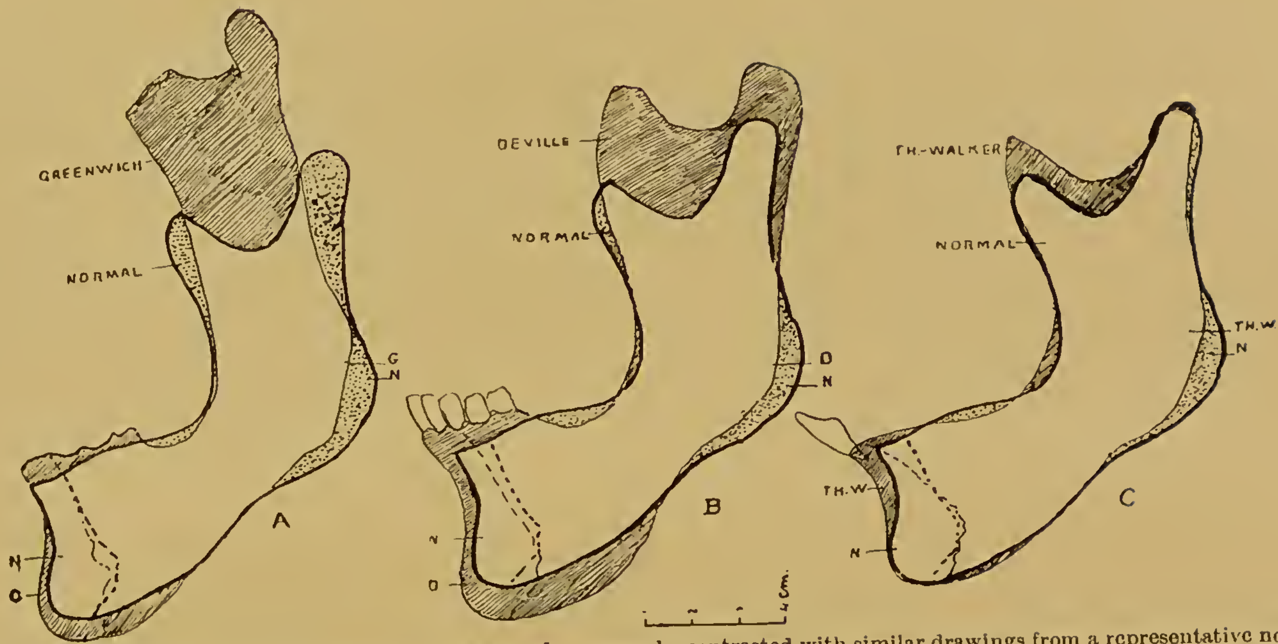
shown. They are founded on measurements made on 21 students at the London Hospital. The mean area of the upper alveolar arcade in the acromegalic is 2720 mm². ; in the English students the mean area is greater—viz., 2800 mm². ; the area of the lower arcade in the acromegalic is 2370 mm². ; in English students 2620 mm².

In giant O'Brien the upper arcade measured 2800 mm^2.; in a gentleman who has suffered from acromegaly for over 20 years it amounts to 2170 mm^2. There is thus a difference of 630 mm^2. between the largest and the smallest palate in the six cases. The area of the palate is actually diminished in the acromegalic, especially that of the lower dental arcade. Fig. 4 also gives the mean lengths and breadths of the palate. Besides a reduction in the size of the lower alveolar area there are also certain constant and well-marked growth changes in the alveolar part of the lower jaw of the acromegalic: (1) The width between the last lower molars is increased in the mean by nearly 10 mm., so that the right and left lower molars in place of being nearer together than the upper are wider apart and project beyond the upper dental arcade (Fig. 4); (2) the canines are advanced so as to come more nearly into a transverse line with the incisors (Fig. 4); (3) porous vascular bone is heaped up on the alveolar margin, elevating the dental sockets. The vault of the hard palate is thus increased; the mean height of the alveolar margin measured from the hard palate opposite the second molar tooth is 17·5 mm. in the acromegalic and 12·5 in English students. Similarly the lower alveolar margin of the mandible is raised, the tooth sockets being elevated at the same time. The separation of the teeth which occurs in acromegaly, is due to the alveolar or socket elevation, not to a linear increase of the alveolar margin. The growth at the alveolar margins and the elevation of the dental sockets I suppose to be stimulated by the pressure brought to bear on those parts during mastication. Pressure cannot influence the linear dimensions of the alveolar arch; that depends on the number and size of the teeth.

Growth Changes in the Mandible.

The results given regarding the palate will surprise those who have noted the great face changes in the acromegalic, especially the underhung protuberant mandible and chin. The cause of the mandibular projection becomes very clear when the growth changes are analysed. The changes are shown in Fig. 5. In Fig. 5 A the mandible of the Greenwich skull is compared with a mandible which may be regarded as normal. As regards the body of the jaw, growth is seen to have taken place (1) in the alveolar margin, (2) on the mental eminence, (3) on the lower margin anterior to the groove for the facial artery. The most remarkable changes are seen in the ramus; the double process of deposition and absorption has completely altered the character of the ramus. It has become markedly narrower; the region of the angle has been absorbed and hence the appearance of an opening out of the angle between the ramus and body of the jaw in the

FIG. 5.



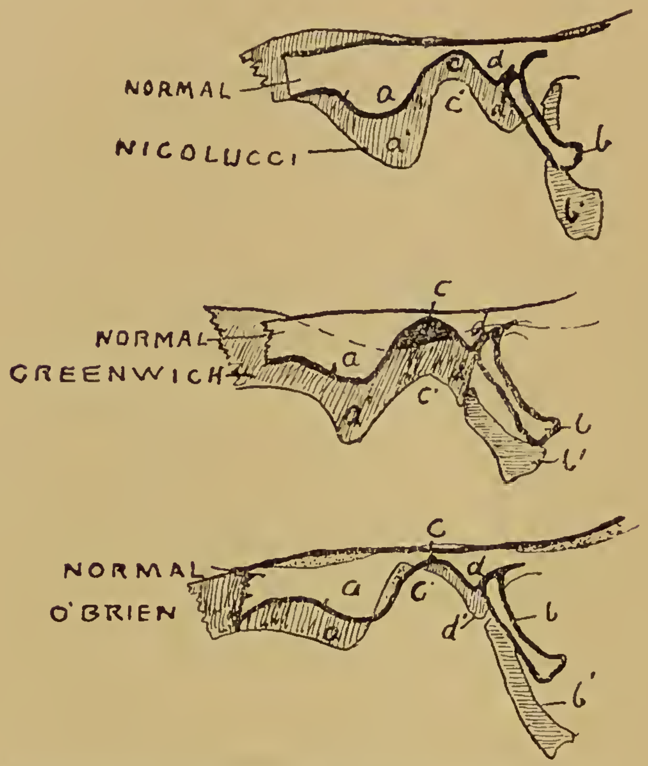
Projection profile drawings of the lower jaw from cases of acromegaly contrasted with similar drawings from a representative normal English skull (indicated by a heavy outline). The stippled areas are those which are absorbed, the shaded those which are deposited. (Half natural size.)

acromegalic. The ascending ramus has increased in height; in place of its height as measured from the lowest insertion of the masseter to the upper surface of the condyle being 65 mm. as in average men, it measures 92 mm.; in the Nicolucci mandible 95; in the gentleman already mentioned 90. The ramus has grown in each of these three cases over an inch in height, and at the same time absorption has been proceeding in the region of the angle. The changes represent exaggerations of the normal process of growth. The condyle, the coronoid process, and the sigmoid notch form the growing edge; growth is taking place at the points of pressure (temporo-maxillary joint) and traction (coronoid process). The whole mandible is being pushed downwards and forwards by the growth at the temporo-maxillary joint, hence the misfit between the lower and the upper teeth. One must remember what such a growth entails: the temporo-maxillary ligaments have to be constantly re-adjusted in their attachments; the masseter and internal pterygoid muscles must also lengthen and alter their insertion. As is well known, the movements at the temporo-maxillary joint become limited. The more the mandible is elongated and depressed the more the temporal muscle acts in the line of the ascending ramus; hence the narrowing of the ramus. Another growth change is not shown in a profile drawing, but is shown when the jaw is examined in a full face drawing (see Fig. 11). Bone is being absorbed from the inner side of the ramus, and being deposited in the outer side at the same time so that the rami appear to move apart, increasing the width of the mouth and pharynx. In normal English jaws the distance from one angle of the mandible to the other varies from 90–98 mm.; in cases of acromegaly the distance is increased, varying from 112–118 mm. The increase is about 14–18 mm. In Fig. 5 B the mandible of the Deville cranium—named after the phrenologist who at one time owned the skull prior to Dr. Barnard Davis—is compared with a normal mandible. The change is not so great as in the three cases just cited, but comparable in amount to the growth change seen in O'Brien's mandible. The Deville cranium is probably also from a giant. In the cranium presented by Mr. Thompson-Walker the changes are slighter; it must be remembered that this specimen is from a Viennese woman and is compared with the mandible of a normal English male. Yet even in this case, one in which a superficial observer would probably say there were no signs of acromegaly, the mandible shows changes of the same nature as in more marked cases.

Changes in the Temporo-maxillary Joint.

As can be readily understood, the growth changes in the condyle of the jaw must affect the temporo-maxillary joint. In all the cases I have had an opportunity of examining such changes are present. The articular eminence is apparently worn away until its anterior part forms merely a margin to the glenoid fossa. (Fig. 6.) When, however, the root of the zygoma is examined it is seen that growth has been in progress on the cranial as well as on the

FIG. 6.



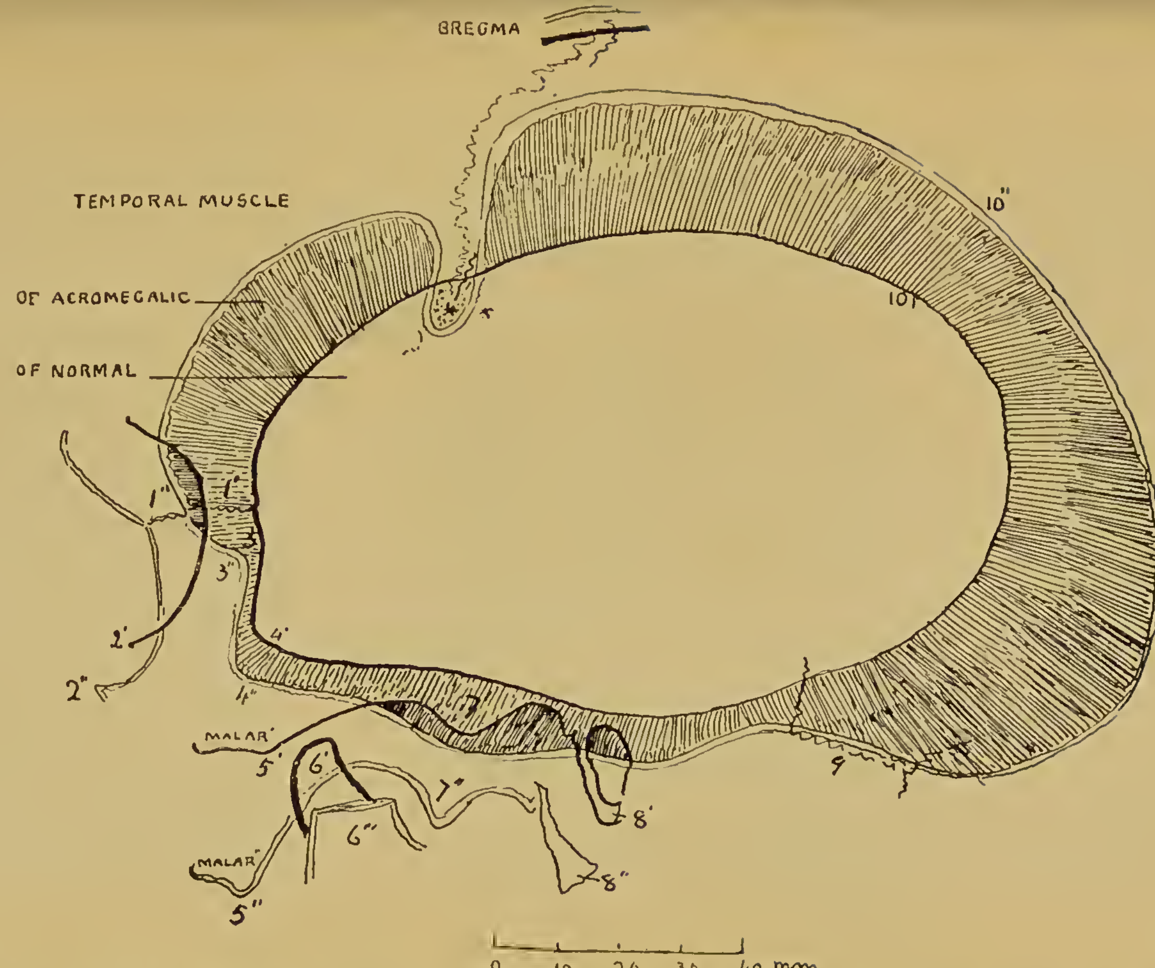
Reconstructions of the temporo-maxillary changes in the acromegalic contrasted with the corresponding parts of a normal skull, three-fourths natural size. *a*, Articular eminence; *b*, Tympanic plate; *c*, Glenoid fossa; *d*, Post-glenoid spine.

mandibular side of the joint. (Fig. 6.) The floor of the glenoid cavity, in place of being 2 or 3 mm. thick, has become from 5 to 8 mm.; the depth of the zygomatic arch as measured from its upper to its lower border at the articular eminence has increased. (Fig. 6.) The limitations in the movements of the mandible are correlated with the changes at the joint.

Changes in the Temporal Fossa and Muscle.

Most remarkable growth changes alter the boundaries of the temporal fossa. (Fig. 7.) At birth the origin of the

FIG. 7.



Comparison of the normal origin of the temporal muscle and boundaries of the temporal fossa with those of the acromegalic. 1′, External angular process of the normal skull; 1″, of the acromegalic; 2′ 2″, Lower margin of the orbit; 3′ 3″, Ascending process of the malar; 4′ 4″, Upper margin of the zygoma; 5′ 5″, Origin of the masseter (lower margin of malar); 6′ 6″, Coronoid process; 7′ 7″, Articular eminence; 8′ 8″, Tympanic plate; 9, Parieto-mastoid suture; 10′ 10″, Temporal ridge (muscular); × Stephanion.

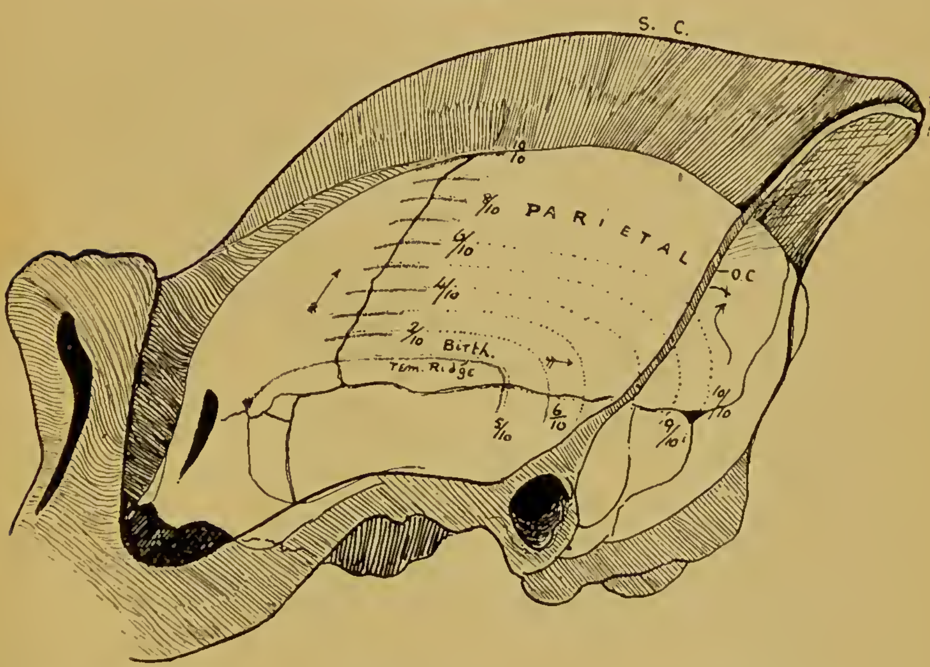
temporal muscle extends only a little way above the lower margin of the parietal bone. As the jaws grow and the teeth appear its origin extends upwards on the side of the skull towards the sagittal suture, preceded by a growing wave of bone—the temporal ridge. At the same time its origin is pushed back towards the lambdoid suture and forwards on the sides of the frontal bone. When acromegaly sets in this process of growth is continued. In Fig. 7 the normal origin of the temporal muscle (unshaded) is contrasted with its origin in a typical acromegalic skull (the Greenwich specimen). *Certain points within the skull were taken as base lines for the purpose of comparison.* The origin of the temporal muscle has extended upwards and backwards on the parietal from 10–25 mm.; the ascent is always arrested at the coronal suture. (Fig. 7*.) The forward growth on the frontal bone leads to most remarkable transformation of the region of the forehead. When viewed in absolute profile the anterior part of the temporal ridge falls 15–20 mm. behind the line of the frontal pole of the brain in normal crania (see Fig. 9), but in acromegaly this ridge may pass forwards until it is in a line with the frontal pole, or may even pass in front of it. (Figs. 2, 3, 7, and 9.) We have here a key to the great growth of the supraorbital ridges and expansion of the frontal sinuses in the acromegalic. The external angular process of the frontal bone and ascending process of the malar—the whole outer wall of the orbit—is actually prolonged or moved forward. (See Fig. 7.) Not only so, but the zygoma in relation to the cranial cavity is lowered, thus increasing the height of the temporal fossa by depressing its floor. (See Fig. 7.) The external auditory meatus in some cases is depressed 10 mm. or more.

Growth Changes in Anthropoids Compared with those seen in Acromegaly.

The key to the growth changes in acromegaly is to be found by studying the corresponding alterations in the crania of growing anthropoids. These changes can be best realised in gorillas. (See Fig. 8.) In anthropoids the cranial cavity has reached almost its full size by the time the animal is four months old. The cranial growth after that period concerns the development of muscular ridges and processes. The temporal muscles spread upwards on the side of the skull until the ridges or waves of bone which precede them fuse along the sagittal suture to form a median crest. (Fig. 8.) They spread backwards until the temporal ridges meet and fuse with the wave of bone which precedes the expanding muscles of the neck to form the occipital crests. (Fig. 8.) The manner in which the temporal fossæ are enlarged by the forward growth of the supraorbital ridges and of the angular and malar processes is shown in Fig. 8. The growth changes in the acromegalic skull are very clearly of the same nature as those which occur in the growing anthropoid.

The growth changes in the upper jaw are also very evident in the gorilla. In Fig. 9 three stages in the growth of the maxillary bone are shown (1) at the fourth year before the first molar tooth has erupted; (2) at the tenth year before the third molar is erupted; (3) when the permanent

FIG. 8.



The growth of muscular ridges and processes in the skull of the gorilla. The skull (unshaded) of a gorilla in which the milk dentition is beginning to appear is placed upon a profile drawing of the skull of an adult male gorilla. Both are drawn to the same scale and are superimposed at corresponding points. The arrows show the direction in which the temporal ridges grow. S.C., Sagittal crest. O.C., Occipital crest.

dentition is complete. The most active centre of growth, as may be seen from Fig. 9, is the posterior part of the maxilla in which the permanent molar teeth are developed. The area of the palate is greatly increased during the eruption of the permanent teeth in the gorilla. In acromegaly the case is the opposite: the size of the palate is rather reduced than increased in area. In some manner the developing teeth supply the stimulus that leads to the development of the palate; in acromegaly this stimulus is absent. During eruption of the teeth the growth of the upper and lower maxillæ is so coördinated that the upper and lower teeth fall into correct apposition. There are at least two factors concerned in this coördination : (1) A substance, evidently derived from the pituitary body which acts on the osteoblasts so that they respond readily to certain stimuli (2) certain forces or stimuli which act directly on the jaws. These stimuli arise from : (*a*) the developing teeth ; (*b*) from pressure applied to the alveoli during mastication ; (*c*) from

FIG. 9.

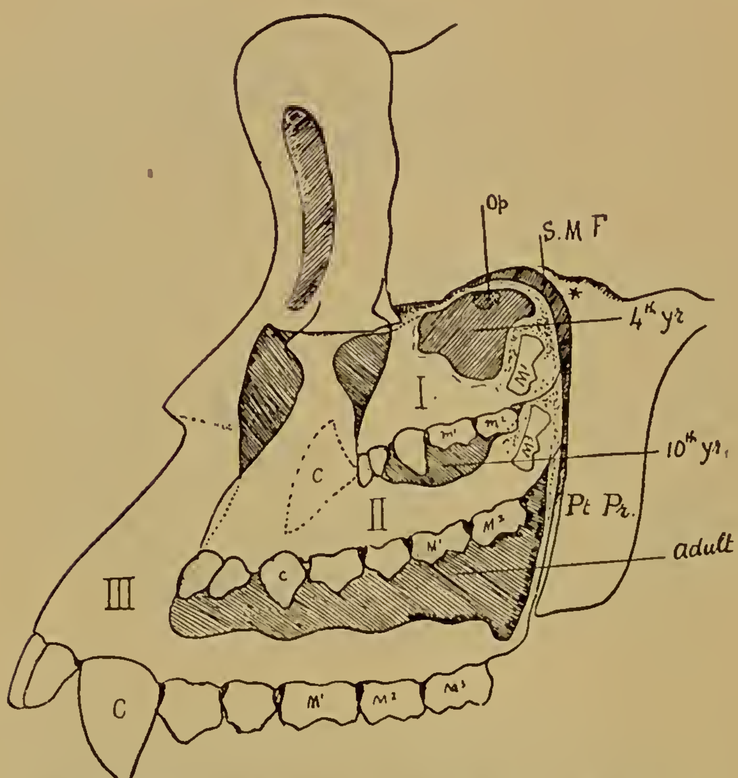


Diagram showing the growth of the upper maxilla and the eruption of the teeth in the gorilla. I., Superior maxilla at the fourth year; II., at the tenth year; III., in the adult. S.M.F., Spheno-maxillary fossa. Pt. Pr., Pterygoid process.

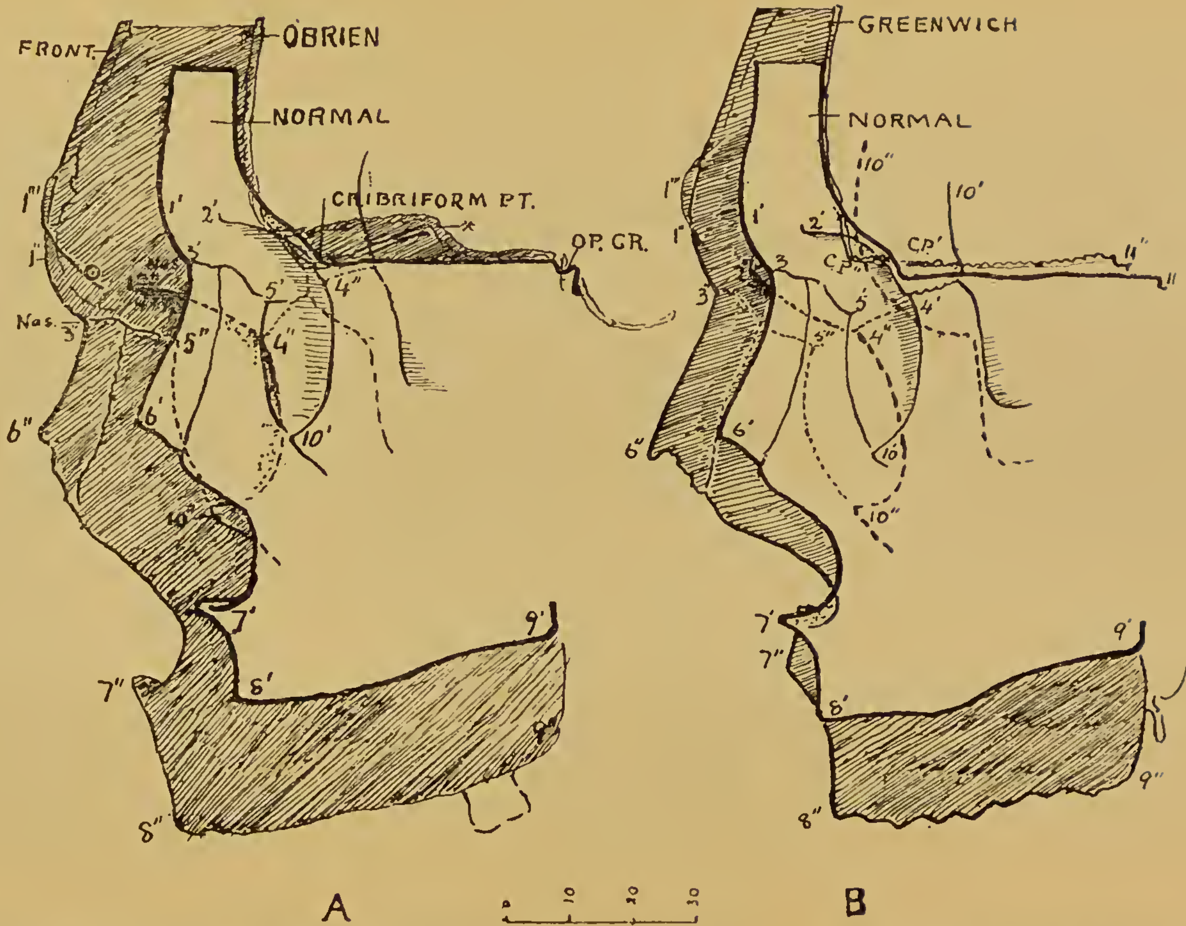
the direct traction of the muscles of mastication. The last-named force acts chiefly on the lower jaw. In acromegaly the sensitising substance is present, and so is the muscular traction, and hence in that disease it is the ascending ramus of the lower jaw that is affected leading to a complete displacement of the lower teeth as regards the upper. In giants in whom the acromegalic condition appears before the eruption of teeth is complete the palatal area does undergo an increase of growth.

Changes in the Forehead and Face of the Acromegalic.

In those who have been the subject of acromegaly for a number of years certain remarkable changes occur in the face—changes which recall the facial characters of the Neanderthal race. In Figs. 10 and 11 these changes are represented diagrammatically—but drawn accurately to scale. I have used the representative English skull already mentioned as the standard for comparison. In Fig. 10 A this cranium is superimposed on that of O'Brien, so that the anterior ends of the cribriform plate of each correspond and so do the upper surfaces of the lesser wings of the sphenoid. The immense thickening and growth of the supraorbital region of the forehead is at once apparent; from the cribriform plate to the glabella of the normal skull the distance measures 14 mm.; in the giant, 34 mm.; in the Greenwich specimen (Fig. 10, B), 25 mm.; in the Nicolucci and Deville specimens, 24 mm.; in the Thompson-Walker specimen (a female), 15 mm. In the giant and Greenwich specimens the frontal sinuses are enormously expanded; in the Thompson-Walker specimen the sinus is very small. The functional meaning of the great growth of the eyebrow region has been already alluded to. The temporal development has caused a forward growth of the orbital region, the external angular process of the frontal and ascending process of the malar coming to occupy a position from 10 to 15 mm. further forwards and downwards than in the normal skull (see Fig. 10, A B).

In acromegaly the nose becomes long and remarkably prominent. It will be observed from Fig. 10 that the nasal bones are very little enlarged, nor is the bridge of the nose more prominent when measured from the lower margin of the orbit. The great development of the supraorbital region of the forehead has forced the root of the nose downwards and forwards. But the nasal prominence is chiefly due to the fact that while the supraorbital region has undergone a remarkable increase in size the palate and maxillary part of the face remain unchanged—at least, as regards its degree of projection or prognathism (see Fig. 10 B). The margin of the pyriform aperture becomes more oblique in position, and this leads to an apparently great increase in its size, whereas in its real height it is little altered. The increase in the length of the upper face is chiefly due to an increase in the depth of the alveolar margin of the maxilla, but, as will be seen presently, the length (or depth) of the malar and upper maxilla is also increased, but to a lesser degree. The length of the upper face as measured from the nasion to the alveolar margin in the English skull, used here as a type, is 73 mm.—3 mm. more than what may be regarded

Fig. 10.



Profile drawing of a representative English skull placed on a corresponding tracing of O'Brien's cranium (A) and on the Greenwich specimen (B) (Two-thirds natural size.) 1′ 1″, Glabella of normal skull and of acromegalic skull; 1′ 1″ 1‴, Supraciliary process; 2′ 2″, Supraorbital margin of the normal and acromegalic crania; 3′ 3″, Nasion; 4 4″, Fronto-malar junction; 5′ 5″, Internal angular process; 6′ 6″, Tip of nose; 7′ 7″, Nasal spine; 8′ 8″, Incisor point of alveolar margin; 9′ 9″, Posterior alveolar tuberosity; 10′ 10″, Anterior part of temporal ridge; 11′ 11″, Optic groove (also OP. GR.); cribriform point is the anterior end of cribriform plate.

as an average. In the Nicolucci specimen it is 90 mm., in the Greenwich 82, in the Deville 83, in O'Brien 83, in the Thompson-Walker 71. In the Neanderthal race, so far as we yet know it, the length of the upper face varies from 80 to 90 mm.—the same as in the acromegalic. As already said, the chief increase affects the depth of the alveolar margin. This increase I regard as being due to the intermittent pressure of mastication, pressure acting as a stimulus to the alveolar margin of the maxilla.

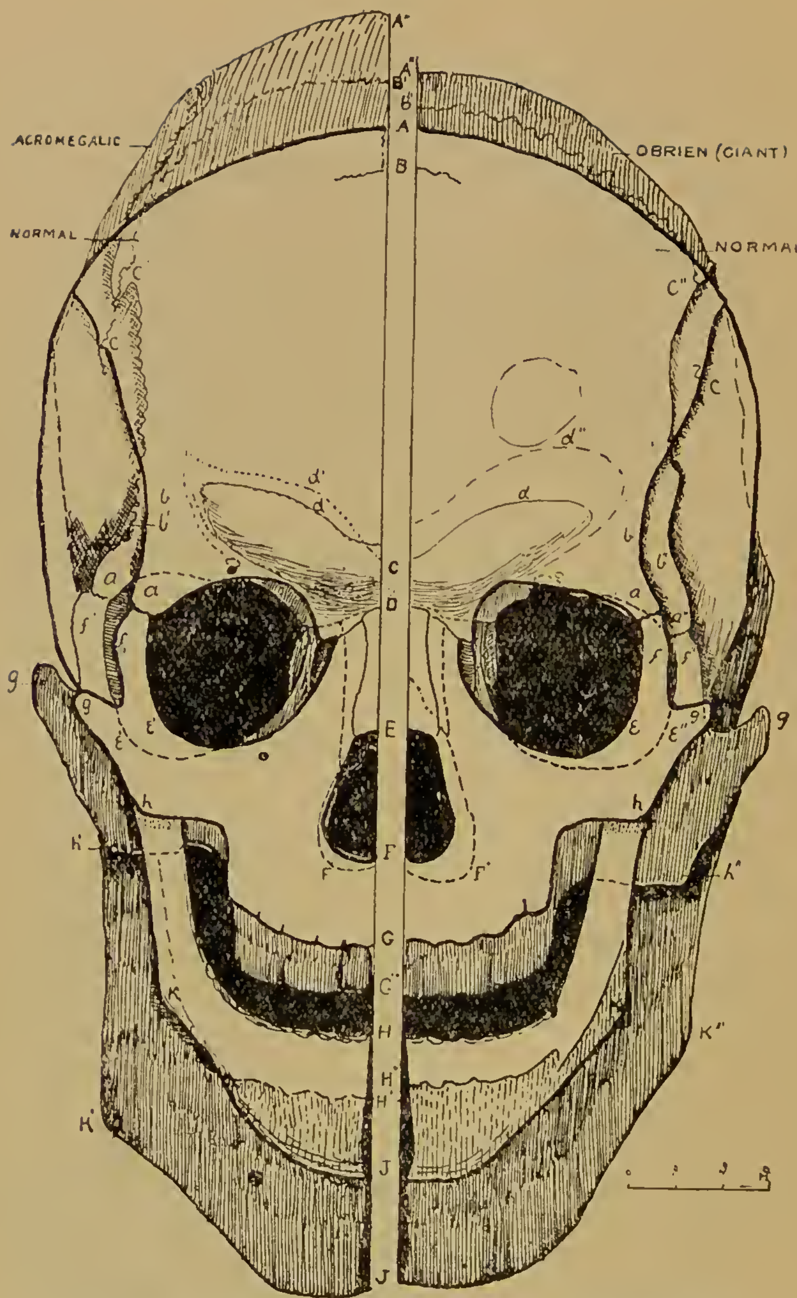
The facial changes in acromegaly are further seen when the face is studied from the front. In Fig. 11 these changes are represented. On the left hand of that figure I have superimposed the normal skull on the Greenwich specimen; on the right hand side on O'Brien's skull. One sees at once there is slight increase in the inter-orbital diameter; it amounts to from 3 to 5 mm. The chief change in the orbit concerns its outer wall. The external angular process of the frontal and the ascending process of the malar move not only forwards, as we have already seen, but also outwards from 8 to 10 mm., thus enlarging the orbits in an outward and downward manner. (Fig. 11.) The increase is connected with the temporal changes already described. The growth of the malar and zygoma is remarkable; they are apparently stimulated by the traction of the masseter, the depth of the body of the malar being increased from 8 to 15 mm. (Figs. 10, 11.) The interzygomatic diameter in the type skull is 129 mm. (130 is the mean measurement); in O'Brien it is 153, in the Deville specimen 150, in the Greenwich 150, in the Nicolucci 154, and in the Thompson-Walker specimen 124. As already said, the last specimen shows many aberrant features. The increase in the depth of the alveolar margin is shown, so are the remarkable changes in the mandible. The depth of the symphysis has increased; the condyles and ascending rami have moved apart. The extent of these changes may be estimated from Fig. 11, which is reproduced one-half natural size. The total increase in face length in well-marked cases of acromegaly is about 20 mm; the increase from one angle of the jaw to the other rather less.

Changes in the Vault and Capacity of the Skull.

Mr. Cecil Beadles [22] noted a fact in connexion with pathological thickening of the vault of the skull which I have verified—viz., that this thickening affects the frontal section of the vault first and most. The process commences in the forehead and spreads backwards. It will be noted further that the thickening along the vault is bounded on each side by the temporal lines. Thus between the origins of the temporal muscles there is built up a strong sagittal arch of

[22] Beadles, Cecil: loc. cit.

FIG. 11.



Drawings of the full face of acromegalic crania compared with the normal. The type skull is shown in outline; the acromegalic are shaded. On the left half of the figure the type skull is superimposed on the Greenwich specimen, on the right half on O'Brien's skull (½ natural size). A, Highest point of vault above the plane of orientation (subcerebral plane, see Fig. 3); B, bregma; C, glabella; D, nasion; E, tip of nose; F, nasal spine; G, alveolar point; H, alveolar point of lower jaw; J, mental eminence.

bone, the anterior part of the arch resting on the supra-orbital bar, the posterior on the external occipital protuberance. The arch provides a strong fulcrum for the origin of the temporal muscles. The arch in the gorilla is similarly strengthened by the high sagittal crest. The thickening of the calvarial sagittal arch I regard as similar in nature to the other changes already mentioned—its formation is correlated with the masticatory changes. In three of the crania the fronto-parietal and fronto-sphenoid sutures were raised up or elevated above the plane of bones as if growth had also occurred in the sutural lines, thus increasing the antero-posterior length of the cranial vault. It is possible there may be a slight increase in the size of the cranial cavity, but the evidence on this point is inconclusive. The mean cranial capacity of the skull of the English male may be taken at 1540 c.c.; in the Deville cranium (a giant's) the capacity is 1650 c.c.; in O'Brien, 1550; in the Greenwich specimen, 1500; in the Nicolucci specimen, 1500; in the Thompson-Walker specimen, 1200 c.c. It is becoming apparent that the capacity of the Neanderthal crania has been under-estimated; they apparently approach the figure given for the Deville cranium.

It is well known that in Paget's disease the calvaria become greatly thickened, measuring from 12–20 mm. The dense outer and inner tables are replaced by porous bone. Along the roof of the skull the bones vary in thickness from 5–7 mm. in normal crania. Mr. Cecil Beadles[23] regarded calvaria in which the average thickness was above 12 mm. as having been subjected to pathological changes. In Neanderthal crania the thickness varies from 8–10 mm. In the six acromegalic calvaria which I examined minutely, the thickness of the frontal and of the parietal bones was the following: Mr. Beadles's specimen, 6 mm., 6 mm.; Greenwich specimen, 6, 8; Nicolucci, 15, 15; the Deville, 10, 10·5; O'Brien, 11, 10; the Thompson-Walker specimen, 12, 13. Thus in two of them the bones were markedly thickened and porous, recalling the condition in osteitis deformans; in two (O'Brien and Deville) the bones were thickened, but, as in Neanderthal calvaria, the outer and inner tables were retained; in two the bones were dense and of normal thickness. The frontal bone suffers the greatest degree of change, and is the first to undergo alteration. In all of these specimens the inner table of the frontal bone, especially above the orbital plates, shows a tendency to the formation of small dense osteomata. A similar formation occurs within the frontal sinuses.

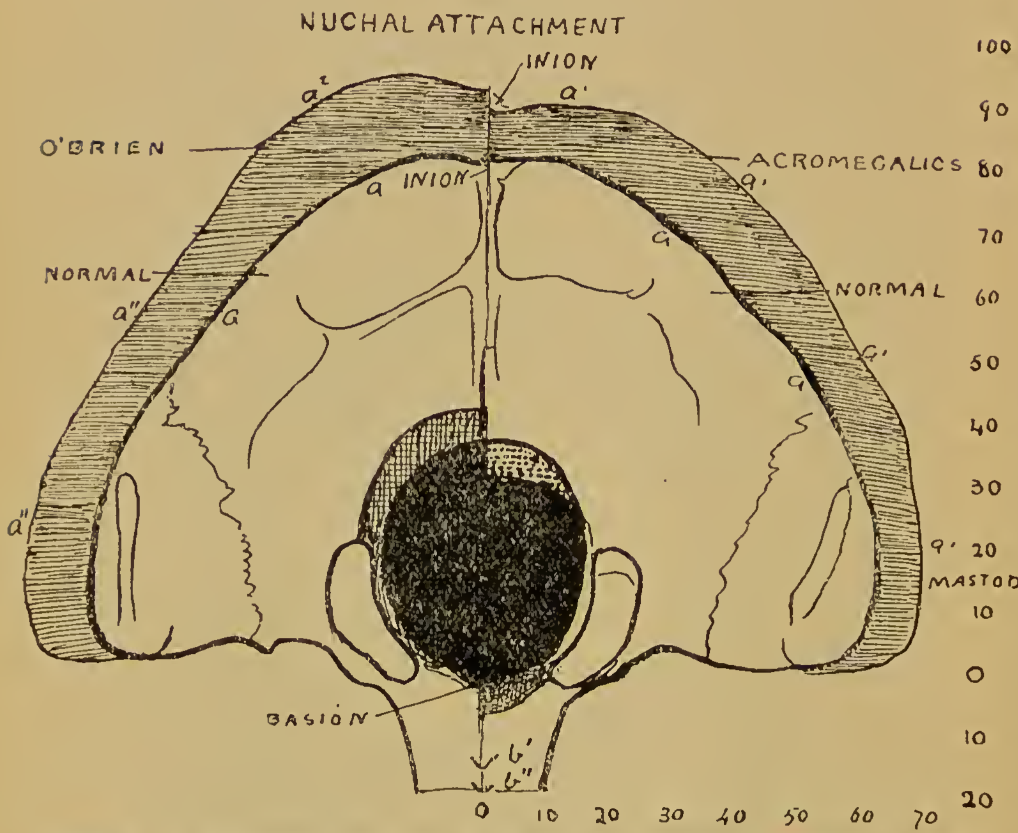
Changes in the Occipital Region of the Skull.

I now turn to the occipital region of the skull which undergoes remarkable and instructive changes in acromegaly

[23] Loc. cit.

—changes which have not been hitherto described nor analysed. It will be remembered that in young anthropoids, as the neck grows in thickness and strength a wave of bone, represented by the upper curved lines on the human skull, expands in front of the growing muscles and forms a wide occipital crest. (Fig. 8.) In acromegaly a similar change occurs. In Fig. 12 is shown the area of a normal English

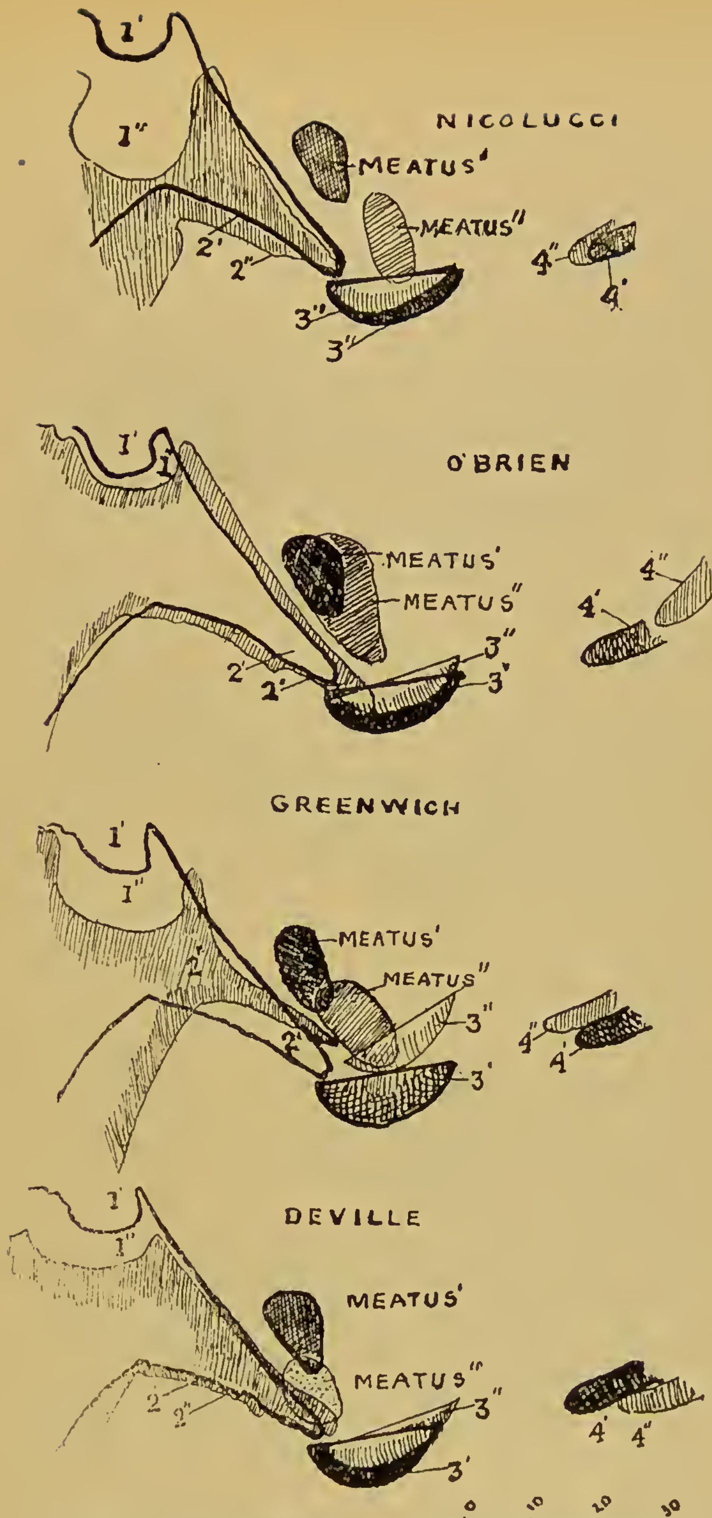
Fig. 12.



The area of attachment of the neck in the type skull (unshaded); the increase in the acromegalic skull is shown by the shaded area (two-thirds natural size

skull to which the neck muscles are attached. On to the right side of the area is placed the corresponding part of the Greenwich skull; on the left half is superimposed the nuchal area of O'Brien's skull. The extent to which these two crania exceed the normal as regards the nuchal area is shown by the shaded marginal area. In acromegaly the muscles of the neck obtain a wider area of attachment. The extent of this area in the type skull is 8120 mm².,

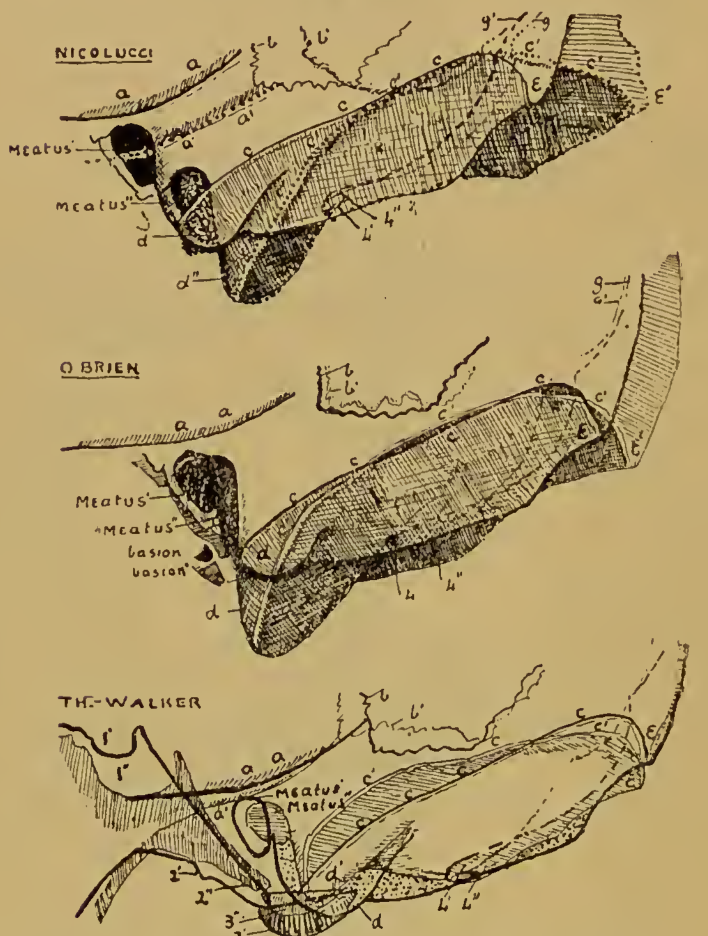
FIG. 13.



Profile drawings showing the basilar process of the skull, pituitary fossa, external auditory meatus, occipital condyles, and foramen magnum of four cases of acromegaly. In each case a drawing of the corresponding parts in a type skull are shown (two-thirds natural size). 1′ 1″, Pituitary fossa of type skull and of acromegalic; 2′ 2″, Basilar process; 3′ 3″, Occipital condyles; 4′ 4″, Occipital bone behind foramen magnum.

in the Greenwich skull 10,320 mm². (an increase of 2200 mm².), and in O'Brien's 10,720 (an increase of 2510). The

FIG. 14.



The growth changes in the occipital region of the skull in acromegaly. The upper drawing represents the changes in the Nicolucci specimen; the middle that in O'Brien (giant), and the lower in Mr. Thompson-Walker's specimen (half natural size). *a' a'*, *a'' a''*. The suprameatal ridge in the normal and in the acromegalic skulls; *b' b'*, *b'' b''*. The parieto-mastoid suture in the contrasted crania; *c' c'*. *c'' c''*. Superior curved line of the occipital of the two crania; *d' d''*, Mastoid process; *e'*, *e''*, External occipital process; *g'*, *g''*, Inner aspect of occipital bone; 1', 1'', Pituitary fossa; 2', 2'', Basilar process; 3', 3'', Occipital condyle; 4', 4'', Occipital behind foramen magnum (opisthion).

inion is moved upwards on the occipital bone from 8 to 10 mm. (exactly as we know is the case in the Neanderthal race) and the mastoid processes are wider apart by 10–25 mm.

There is also a change in the position of the foramen magnum. In the giant's skull, and also in the Deville skull, which I believe also to be that of a giant, the foramen is moved backwards by a growth of the basilar process, as in the Neanderthal man ; in the acromegalic crania of adults the foramen magnum is moved forwards owing to a remarkable atrophy of the basilar process of the occipital. These changes in the occipital region are illustrated also in Fig. 13. The posterior part of the base of the skull, including the pituitary fossa, is drawn to scale. The thickened outline represents the type skull, the thin shaded outlines the acromegalic. The atrophy of the basilar process in the Nicolucci and Greenwich specimens is apparent; in the giants' skulls the process is increased in length. The growth changes have altered the position of the auditory meatus. Bone has been added to the orifice so that the meatus is deeper and enlarged, but its position is also shifted ; it has moved downwards and backwards as regards the basal part of the skull. The occipital condyles have also changed—a change which is more marked in the Greenwich specimens than in the others. The condyles are reduced in size ; their axis is altered so that the head is carried in a more extended position ; they are also pressed upwards into the base of the skull, as if the base had become softened and yielded somewhat. These changes are constant in the later and atrophic phases of acromegaly.

Other changes in the occipital region of the skull are shown in Fig. 14. Profile drawings of three acromegalic skulls are superimposed on corresponding outlines of a normal skull. The upper drawing shows the Nicolucci skull, and the changes in the Greenwich specimen are identical to those shown in this specimen. The root of the zygoma has been shifted, as regards the interior of the skull, downwards and backwards quite half an inch (12 mm.). These changes are correlated with the enlargement of the temporal fossa already described. The mastoid process is elongated, the area for the attachment of the neck muscles has been extended backwards by a deposit of bone in the region of the occipital protuberance ; the line of attachment represented by the superior curved line assumes a more oblique position as regards the horizontal plane of the skull. The changes in the O'Brien and Deville crania are similar in character but less in extent. This is also true of the Thompson-Walker specimen. These alterations in the occipital region of the skull are similar in nature to those which I have described in the crania of growing anthropoids.[24]

[24] Keith, A. : Journal of Anatomy and Physiology, 1910, vol. xliv., p. 251.

Growth Changes in other Parts and Systems of the Body.

The space at my disposal precludes a detailed description of the changes in the rest of the skeleton. They are of the same nature as in the skull—wherever there is traction applied by ligaments, or by muscles, or pressure applied, as in standing or walking, growth takes place in the part of the skeleton on which the various forms of force act. Atrophy is also at work—especially in the cancellous tissue, for it seems that growth and absorption are necessarily correlated. The atrophy especially affects the tarsus and bodies of the vertebræ. There are kyphosis and flat-foot in all cases of acromegaly of long standing.

All the systems of the body are affected, and this is especially true of the vascular system. John Hunter realised the close relationship between vascular formation and bone deposit. The growth of bone, such as we have seen occurs in acromegaly, implies an active formation of vessels. The osseous vascular system in acromegaly becomes markedly altered ; the capillaries, and especially the venous sinuses, increase in number and in size. The surfaces of the bones become pitted and marked by vascular foramina and impressions. All the veins in and below the base of the skull dilate, especially the emissary veins. The small venous foramina open out, and one of them, the cranio-pharyngeal canal, the closed track of the developing pituitary body, may open up. It often does ; in most anthropoids it remains open. It is open in O'Brien as in giants generally and in many cases of acromegaly, but in my interpretation it is not a congenital persistence betokening an inherent defect in the pituitary, but a dilatation of a minute vascular channel which is to be seen in the normal skull. All such venous vascular channels are dilated.

The connective tissue of the body increases, especially round the sheaths of nerves. This was markedly the condition in Dr. G. A. Gibson's case, the post-mortem examination of which has been so well described by Professor A. Campbell Geddes.[25] The skin hypertrophies. A formation of small fibrous pendulous molluscous tumours on the side of the neck is very common. In many cases there is a hypertrophy of viscera.

It would take one too far afield to summarise the present position of our knowledge of acromegaly. That has been excellently done by Sir David Ferrier, Kohn, and Münzer. From the surgical point of view recent articles by Dr. Harvey Cushing[26] and Professor Eiselsberg[27] should be consulted.

[25] Geddes, A. C. : Edinburgh Medical Journal, 1909, N. S., vol. ii., p. 218.

[26] Cushing, H.: Journal of the American Medical Association, 1909 vol. liii., p. 249.

[27] Eiselsberg, F. von : Annals of Surgery, 1910, vol. lii., p. 1.

The two points which I wished to bring forward evidence to prove in this paper were the following:—1. That the changes in acromegaly are of the nature of true growth, and are apparently due to the circulation through the body of a substance formed in the pituitary. This substance seems only to sensitise the tissues, the actual cause of their growth being mechanical stimuli arising from muscular action and mechanical movement. 2. The growth changes seen in the acromegalic are of the same nature as those which occur normally in anthropoids and in the Neanderthal race, and both are probably due to a condition of hyperpituitarism.